REMARKS

Support for the Claim Amendments

Claim 18, 19, and 20 are amended to recite specific features of the macromers that confers compliance in the resulting hydrogels. Support for the amendments may be found in the specification as published at least at paragraphs 19 to 33 and 50, more particularly paragraph 19, lines 12& 13, paragraph 21 lines 8, paragraph 25 line 3, and paragraphs 32 and 33, Examples 4 & 5 and corresponding figures 2A&B which describe the requirement that the hydrogels be compliant and the macromers structure as comprising carbonate linkages.

Claim 23 is amended to define the formulation as comprising a polymerization initiator. Support for this amendment can be found in the specification as published at least at paragraphs 36-39, and 92.

Applicant thus submits that these amendments do not introduce new matter. Accordingly, Applicant respectfully requests that these amendments be entered.

Rejection of claims under 32 USC §103(a)

1. Claims 18-26 were rejected under 35 USC §103(c) as being unpatentable over Sawhney I (US5900245) in view of Sawhney II (US6,605,294) and Levy et al. (US5387419). Applicant hereby amends the claims to more clearly point out that the claimed compositions are liquid aqueous formulations of macromers that form compliant hydrogels upon polymerization. The claimed compositions recite the macromers with features that contribute to the compliance attributes of the polymerized gels. Applicant respectfully submits that the present claims are patentable over the cited art as the references lack the required incentive for the cited combination.

Specifically, while Sawhney I teaches the general delivery of drugs from its hydrogels, it does not teach or suggest compositions for the delivery of drugs to treat arrhythmia or compositions for the delivery of drugs in particulate form from aqueous formulations of macromers as claimed that forms compliant hydrogels. Further, Sawhney I, alone, does not

render the present invention obvious as a skilled artisan reading Sawhney would have no knowledge, nor any kind of expectation, as to how the mixing of particulate materials into the Sawhney I formulations of macromers would affect the compliance in the resulting hydrogel. Applicant had pointed out in a prior response how a skilled artisan apprised of the teachings of Sawhney I would not derive how the mechanical properties of the resulting hydrogel, such as compliance or adherence, would be affected by the presence of the particles within the gel or the initial macromer formulation. Thus a skilled artisan reading Sawhney I alone would not be motivated to prepare the aqueous formulations presently claimed used to form compliant hydrogels for the delivery of drugs to the heart.

A skilled artisan trying to improve upon the deficiencies of Sawhney I's formulations for forming hydrogels would not be motivated to look to the teachings of Sawhney II as Sawhney II merely teaches uses of hydrogels as plugs to seal voids or tracks. Sawhney II does not teach any specific formulations of macromers with anti-arrhythmic drugs, less any that would form compliant hydrogels. Indeed, unlike the hydrogels derived therefrom, aqueous formulations of macromers do not have the needed tensile modulus and swelling properties required to fill voids (see Sawhney II col. 9, lines 9-20). Also, compliance is not a concern of Sawhney II, as the hydrogels are not meant to be deposited on surfaces of the heart but meant to fill holes made in an organ. Because Sawhney II is not concerned with compliance of the formed gel, he provides no guidance as to how to retain or overcome the effects the load of particles would have on the formed gels with regard to compliance. He makes no suggestions on how to modify formulations or macromer structures to retain compliance.

Applicant notes the examiner's reference to Sawhney II col. 8 and example 1. These teachings of macromers do not include macromer compositions and formulations as presently claimed wherein the macromer comprises carbonate linkages.

Applicant notes the examiner's reference to Sawhney II col. 13, line 67 which lists anti-arrhythmic agents. However, this term merely appears among a long list of classes of biological activities in reference to water-soluble drugs to be incorporated into hydrogel articles, not particles or formulations of macromers, respectively (see opening sentence at line 61).

Applicant also notes the reference to Sawhney II col. 14, line 15 that teaches that "The biologically-active agent may be ... insoluble in the polymer solution to form suspension or dispersion". This being the only reference to "a polymer solution" in combination with a drug in Sawhney II (the remainder being mostly concerned with hydrogels), it would be unclear to the skilled artisan what that solution or polymer might be.

Thus, each and all of these passages do not amount to a teaching that would satisfactorily provide the required motivation to combine these teachings with those of Sawhney I as proposed by the examiner. At best, these passages amount to a mere invitation to try experimentation, but provide little guidance to the skilled artisan as to which particular biologically-active agent in which polymer solution will yield a suitable composition.

Thus, a skilled artisan apprised of the teachings of Sawhney II would not have any motivation to modify its teachings with those of Sawhney I to arrive at the presently claimed inventions nor any expectation that, in doing so, he/she would succeed.

Likewise, a skilled artisan trying to improve upon the deficiencies of Sawhney I's formulations or Sawhney II's hydrogels would not be motivated to look to the teachings of Levy as Levy effects control of the delivery of the drug by relying on the hydrophobic nature of the polymeric matrices to slow the diffusion of the drug into the tissue and the absorption of the aqueous body fluid within the matrices. Indeed, while Levy teaches compositions for the treatment of arrhythmia, Levy nonetheless fails to cure all the deficiencies of Sawhney I or Sawhney II in that it also does not teach or suggest compositions for the delivery of drug particles from aqueous formulations that form compliant hydrogels. The polymeric matrices taught in Levy are either 1) hydrophobic matrices (see col. 3, lines 18-33; col.5, line 56 to col. 6 line10) or 2) in the case of collagen (col. 3, line 32; col. 6, line 9), not covalently reactive macromers polymerizable to form a compliant tissue hydrogel; they do not contain macromers capable of crosslinking to form compliant hydrogels. The processes taught in Levy do not concern the suspension of particles of a drug in aqueous formulations. They mostly concern the formation of blends between hydrophobic polymers and the drug either in neat form or optionally with the assistance of an organic solvent in which both the drug and the polymer are soluble (see col. 3

line 47-60; col. 7, line 53 to col. 8 line 8). Levy formulations with an organic solvent are clearly not intended for direct implantation within the body as these formulations are either not biocompatible (see examples 3, 8, 9, and 10 (dimethylacetamide), example 4 (chloroform, methylene chloride and ethylacetate), and example 11 (methylene chloride and acetic acid)), or further taught to be cast into films or molded into substrate shape (see col. 4, lines 1-8; and examples 1, 2, 3, 8, 10, 11). Levy constantly refers to these compositions as either films or substrates indicative that these matrices are not in the form of aqueous solutions nor hydrogels.

Accordingly, the cited references are not combinable as neither Sawhney I, Sawhney II, nor Levy teaches or suggests modification to their compositions to arrive at the presently claimed compositions. Applicant respectfully requests that this rejection be withdrawn.